

FIGURE 7

Amino acid sequence alignment of variants of selected scFv antibodies against loop 6 of human CCR5

V_H region:

| | CDR1 | CDR2 | CDR3 |
|-----------|--|------|---------|
| 15.150.11 | QVQLQESGPGLVKPSSETLSLTCTVSGGSI--GHDYWSWIRQPPGEGLEWIGFIFFDGSNTYNPNSLNGRVTISLDTSKNQLSLRLTSVTAADTAIFYCARLKGAWLLSEPPYPFSSDGMVDVWGQGT | | TTVTVSS |
| 15.150.12 | QVQLQQWGAGLLKSWGTLSLTCAVSGASF--SGYYWSWIRQPPGKGLEWIGIENHRGSTTYNPSLDGRVTISLDTSTNQISLKLTSMTAADTAIFYCART-----VAGTSDYWGQGT | | TLVTVSS |
| 15.150.24 | QVTLKESGPTLVKPTQTTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPSLKSRLTITKDTSKKQVVLTMNTNVDPADTATYYCTHEQYYDYDTSGQPY-----FDFWGQGT | | TLVTVSS |

V_L region:

| | CDR1 | CDR2 | CDR3 | |
|-----------|-----------------------|--|--|---------|
| 15.150.11 | NFMLTQPPS-ASGTPGQRVSI | SCSGSSS-DIGSNTVNWYQQLPGTAPKLLIYSNNQRP | SGVDPDRFSGFKSGTSASLVISGLQSEDEADYYCAAWDESLNGVWVFGG | GTKVTVL |
| 15.150.12 | ETTLTQSPAFMSATPGDKVSI | SCKASR--DVDDD-VNMYQQRPG | EAPIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDSEDAAYYFCLQHDNF--PLTFGGG | GTKVEIK |
| 15.150.24 | NIQVTQSPSSLSASVGD | RVMTTCRASQ--DI-RKNLNWYQQRPGKAPKVLIDASDLETGIPSRFSGSGSGTDFILTISSLPEDIA | TYCCQSD-YL-PLTFGGG | GTKVDIK |

Handwritten notes: "1/2" and "2/2" with arrows pointing to the CDR3 regions of the V_H and V_L sequences respectively.

FIGURE 8

Amino acid sequences of variable regions of clone 15.186.35 scFv against N-terminus fragment of human CCR5

V_H region [SEQ ID NO: 34]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSSTSGVSVGWIRQPPGKALEWLASINWNDDKCYSPLKSRITITKDTPKNQV
VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPGTMVTVSS

V_L region [SEQ ID NO: 35]:

SYELMQLPSVSVSPGQTASITCSGDNLGDKYACWYQQKGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAM
DEADYYCQAWDTSTAVFGTGKLTVL

Partial amino acid sequences of variable regions of clone 15.150.11 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 36]:

QVQLQESGPGLVKPSSETLSLTCTVSGGSIGHDYWSWIRQPPGEGLEWIGFIFFDGSTNYPNPSLNGRVTISLDTSKNQLSL
RLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMVWGQGTTVTV

V_L region [SEQ ID NO: 37]:

NFMLTQPPSAXGTPGQRVSISSGSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGFKSGTSASLVISGLQ
SEDEADYYCAAWDESLNGVVFGGG

Partial amino acid sequences of variable regions of clone 15.150.12 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 38]:

QVQLQQWGAGLLKSWGTLTLTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYPNPSLDGRVTISLDTSTNQISL
KLTSMTAADTAVYYCARTVAGTSDYWGQGTTLTVSS

V_L region [SEQ ID NO: 39]:

TTLTQSPAFMSATPGDKVSISSCKASRDVDDVDVNWYQQRPGEAPIFIIEDATTLPVGPISPRFSGSGYGTDFTLTINNIDS
EDAAYYFCLQHDNFPLTFGGGKTKVEIK

Amino acid sequences of variable regions of clone 15.150.24 scFv against loop 6 fragment of human CCR5

V_H region [SEQ ID NO: 40]:

QVTLKESGPTLVKPTQTLTLTCTFSGFSLRITGEGVGWVRQPPGKALEWLALIYWDDDKRYSPLKSRITITKDTSKKQV
VLTMTNVDPADTATYYCTHEQYYDTSGQPYYFDFWGQGTTLTVSS

V_L region [SEQ ID NO: 41]:

NIQVTQSPSSLSASVGDRTMTTCRASQDIRKNLNWYQQKPGKAPKVLIDYASDLETGIPSRFSGSGSGTDFILTISLQP
EDIATYYCQQSDYLPLTFGGGKTKVDIK

#4

FIGURE 1A

Amino acid sequence of human CCR5 [SEQ ID NO: 1]:

1 MDYQVSSPIY DINYYTSEPC QKINVKQIAA RLLPPLYSLV FIEGFVGNML VILILINCKR
N-Terminus Transmembrane Domain 1

61 LKSMTDIYLL NLAISDLFFL LTVPFWAHYA AAQWDFGNTM CQLLTGLYFI GFFSGIFFII
LOOP 1 Transmembrane Domain 2 Loop 2 Transmembrane Domain 3

121 LLTIDRYLAV VHAVFALKAR TVTEGVTSTV ITWVVAVFAS LPGIIFTRSQ KEGLHYTCSS
Loop 3 Transmembrane Domain 4 Loop 4

181 HFPYSQYQFW KNFQTLKIVI LGLVLPLLVM VICYSGILKT LLRCRNEKKR HRAVRLIFTI
Transmembrane Domain 5 Loop 5

241 MIVYFLFWAP YNIVLLLNTF QEFFGLNNCS SSNRLDQAMQ VTETLGMTHC CINPIIYAFV
Transmembrane Domain 6 Loop 6 Transmembrane Domain 7

301 GEKFRNYLLV FFQKHIAKRF CKCCSIFQQE APERASSVYT RSTGEQEISV GL
C-Terminus

FIGURE 1B

Peptide fragments derived from human CCR5 that are used as target peptides:

N-terminal fragment [SEQ ID NO: 8]:

MDYQVSSPIYDINYYTSEPCQKINVKQIAARLLPPL

Loop 4 fragment [SEQ ID NO: 9]:

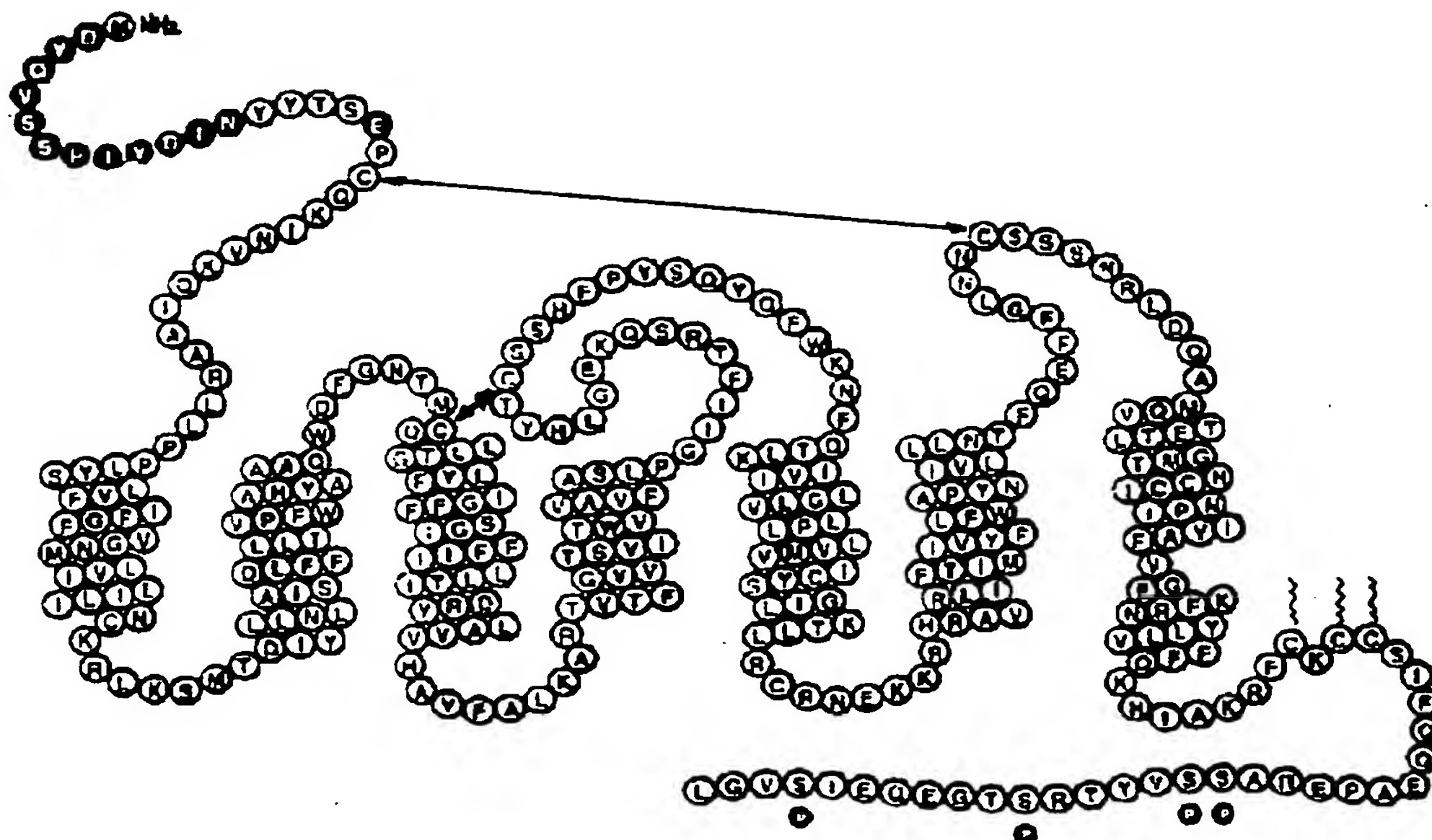
TRSQKEGLHYTCSSHFPYSQYQFWKNFQTLKI

Loop 6 fragment [SEQ ID NO: 3]:

EFFGLNNCSSSNRLDQAMQVTETLGMTHC

FIGURE 1C

A model of the secondary structure of human CCR5:

[illegible]

QVTLKESGPTLVKPTQTLTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPSLKSRLTITKDTSKKQV
VLTMTNVDPADTATYYCTHEQYYYDTSGQPYFYDFWQGQTLVTVSSGGGGSGGGGSGGGGSGGGGSNIQVTQSPSSLSAS
VGDRVMTTCRASQDIRKNLNWYQQKPGKAPKVLIIYDASDLETGIPSRFSGSGSGTDFILTISSLPEDIATYYCQQSDYL
PLTFGGGGTKVDIK

FIGURE 5

DNA sequence of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 16]:

CAGGTTACCTTGAAGGAGTCTGGTCCTACGTTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTGTCTGGGTT
CTCACTCAGCACTAGTGGAGTGAGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTTGAGTGGCTTGCAAGCATAA
ATTGGAATGATGATAAGTGCTACAGCCCATCTCTGAAAAGCAGGCTCACCATACCAAGgACACCCCCaAAAACCAGGTG
GTCCTTGCAATGAGCAACATGGACCCTGCGGACACAGCCACATATTCCTGTGCACTCGATATGCCCCCCCATGATAGTGG
CCCGCAATCTTTTGATGCTTCTGATGTCTGGGGCCCAGGGACAATGGTCACCGTCTCTTCAGGCGGTGGTGGATCAGGCG
GCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTTCCTATGAGCTGATGCAGCTACCCTCAGTGTCCGTGTCC
CCAGGACAGACAGCCAGCATCACCTGCTCTGGAGATAATTTGGGGGATAAATATGCCTGCTGGTATCAACAGAAGCCAGG
CCGGTCCCCTGTGCTGGTCATTTATGGAGATAACAAGCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACCTCTG
GGAACACAGCCACTCTGACCATCAGCGGGACCCAGGCTATGGATGAGGCTGACTATTACTGTCAGGCGTGGGACACCAGC
ACTGCTGTCTTCGGAAGTGGGACCAAGCTCACCGTCCTA

Amino acid sequence of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 17]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSSTSGVSVGWIRQPPGKALEWLASINWNDDKCYSPLKSRLTITKDTPKNQV
VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPGTMVTVSSGGGGSGGGGSGGGGSGGGGSSYELMQLPSVSVS
PGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGDNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQAWDTS
TAVFGTGTKLTVL

DNA sequence of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 18]:

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACTTGCAGTGTCTCTGGTGG
CTCCATCGGTTCATGACTACTGGAGCTGGATACGGCAGCCCCCAGGGGAGGGACTGGAGTGGATTGGTTTCATCTTCTTCG
ATGGGAGACCAACTACAACCCCTCCCTCAACGGTCGAGtCACCATCTCACTCGACACGTCGAAGAATCAGCTCTCCCTG
AGGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTATTTCTGTGCGAGACTAAAGGGGGCGTGGTTATTGTCTGAACC
CCCTTACTTCAGCTCCGACGGCATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCCCCTCAGGCGGTGGTGGATCAG
GCGGCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAATTTTATGCTGACTCAGCCCCCTCAGCGTCTGGG
ACCCCCGGGCAGAGGGTCAGCATCTCTTGTCTGGGAGCAGCTCCGACATCGGAAGTAATACTGTAAACTGGTACCAGCA
ACTCCCAGGAACGGCCCCCAAACCTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCT
TCAAGTCTGGCACCTCAGCCTCCCTGGTCATCAGTGGCCTCCAGTCTGAGGATGAGGCTGATTATTATTGTGCAGCATGG
GATGAGAGCCTGAATGGTGTGGTGTTCGGCGGAGGACCAAGG

Amino acid sequence of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 19]:

QVQLQESGPGLVKPSSETLSLTCTVSGGSIGHDYWSWIRQPPGEGLEWIGFIFFDGSTNYNPSLNGRVTISLDTSKNQLSL
RLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMDVWGQGTTVTVPSGGGGSGGGGSGGGGSGGGGSNFMLTQPPSASG
TPGQQRVSISSGSSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGFKSGTSASLVISGLQSEDEADYYCAAW
DESLNGVVFGGPR

FIGURE 6 (cont.)

DNA sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 28]:

CAGGTGCAGCTACAGCAGTGGGGCGCAGGACTGTTGAAGTCTTGGGGAACCCTGTCCCTCACCTGCGCTGTCTCTGGTGC
GTCGTTTAGTGGTtATTATTGGAGCTGGATCCGCCAGCCCCAGGgAAGGGGCTGGAGTGGATTGGGGAGATCAATCATC
GTGGAAGCACTACCTACAACCCGTCCCTCGACGGTCGAGTCACCATATCATTAGACACATCTACCAACCAGATCTCCCTT
AAACTGACCTCTATGACCGCCGCGGACACGGCCGTGTATTACTGTGCGAGGACAGTGGCTGGTACTAGTGACTACTGGGG
CCAGGGAACCCTGGTCACCGTTTCCTCAGGGAGTGCATCCGCCCAACGGGCGGTGGTGGATCAGGCGGCGGAGGATCTG
GCGGAGGTGGCAGCGGTGGTGGAGGCAGTGAAACGACACTCACGCAGTCTCCAGCATTTCATGTCAGCGACTCCAGGAGAC
AAAGTCAGCATCTCCTGCAAAGCCAGCCGAGACGTTGATGATGATGTGAAGTGGTACCAACAGAGACCAGGAGAAGCTCc
TATTTTtATTATTGAAGATGCTACTACTCTCGTTCcTGGAATCTCACCTCGATTTCAGTGGCAGCGGGTATGGAACCGATT
TTACCCTCACAATTAATAACATCGATTCTGAGGATGCTGCATATTATTTCTGTCTACAACATGATAATTTCCCGCTCACC
TTCGGCGGAGGGACCAAGGTGGAGATCAAA

Amino acid sequence of a variant of clone 15.150.12 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 29]:

QVQLQQWGAGLLKSWGTLSTCAVSGASFSGYYWSWIRQPPGKGLEWIGEINHRGSTTYNPSLDGRVTISLDTSTNQISL
KLTSMTAADTAVYYCARTVAGTSDYWGQGLVTVSSGSASAPTGGGSGGGGSGGGGSGGGGSETTLTQSPAFMSATPGD
KVSISCKASRDVDDVDNWDYQQRPGEAPIFIIEDATTLVPGISPRFSGSGYGTDFTLTINNIDSEDAAYYFCLQHDNFPLT
FGGGTKVEIK

DNA sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 30]:

CAGGTCACCTTGAAGGAGTCTGGTCCTACGCTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTCTCTGGGT
CTCACTCAGAATACTGGAGAGGGTGTGGGCTGGGTCCGTCAGCCCCAGGAAAGGCCCTGGAATGGCTTGCACTCATTT
ATTGGGATGATGATAAGCGCTACAGCCCATCTCTGAAGAGCAGGCTCACCATCACCAAGGACACCTCCAAAAAGCAGGTG
GTCCTTACAATGACCAACGTGGACCCAGCGGACACAGCCACCTATTACTGTACACACGAGCAATACTATTATGATACTAG
TGGTCAGCCATACTACTTTGACTTCTGGGGCCAGGGCACCTGGTCACCGTCTCCTCAGGCGGTGGTGGATCAGGCGGCG
GAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAACATCCAGGTGACCCAGTCTCCATCCTCCCTGTCTGCATCT
GTAGGAGACAGAGTCACCATGACTTGCCGGGCGAGTCAGGACATTAGGAAGAATTTAAATTGGTATCAGCAAAAACCAGG
GAAAGCCCCTAAGGTCCTGATCTACGATGCATCCGATTTGGAAACAGGGATCCCATCAAGGTTTCAGTGAAGTGGATCTG
GGACAGATTTTATCCTCACCATCAGCAGCCTGCAGCCTGAAGATATTGCAACATACTACTGTCAACAGTCTGATTATTTA
CCGCTCACTTTTCGGCGGAGGGACCAAGTGGATATCAAA

Amino acid sequence of a variant of clone 15.150.24 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 31]:

QVTLKESGPTLVKPTQTLTLTCTFSGFSLRTTGEGVGWVRQPPGKALEWLALIYWDDDKRYSPLKSRILTITKDTSKKQV
VLTMTNVDPADTATYYCTHEQYYIDTSGQPYFDFWGQGLVTVSSGGGSGGGGSGGGGSGGGGSNIQVTQSPSSLSAS
VGDRVMTCRASQDIRKNLNWYQQKPGKAPKVLIDASDLETGIPSRFSGSGSGTDFILTISLQPEDATYYCQQSDYL
PLTFGGGTKVDIK

FIGURE 6

DNA sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 24]:

CAGGTCACCTTGAAGGAGTCTGGTCCTACGTTGGTGAAACCCACACAGACCCTCACGCTGACCTGCACCTTGTCTGGGTT
CTCACTCAGCACTAGTGGAGTGAGTGTGGGCTGGATCCGTCAGCCCCCAGGAAAGGCCCTTGAGTGGCTTGCAAGCATAA
ATTGGAATGATGATAAGTGCTACAGCCCATCTCTGAAAAGCAGGCTCACCATCACCAAGgACACCCCCaAAAACCAGGTG
GTCCTTGCAATGAGCAACATGGACCCTGCGGACACAGCCACATATTCCTGTGCACTCGATATGCCCCCCCATGATAGTGG
CCCCGAATCTTTTGATGCTTCTGATGTCTGGGGCCCAGGGACAATGGTCACCGTCTCTTCAGGCGGTGGTGGATCAGGCG
GCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTTCCTATGAGCTGATGCAGCTACCCTCAGTGTCCGTGTCC
CCAGGACAGACAGCCAGCATCACCTGCTCTGGAGATAATTTGGGGGATAAATATGCCTGCTGGTATCAACAGAAGCCAGG
CCGGTCCCCCTGTGCTGGTCATTTATGGAGATAACAAGCGGCCCTCAGGGATCCCTGAGCGATTCTCTGGCTCCAACCTCTG
GGAACACAGCCACTCTGACCATCAGCGGGACCCAGGCTATGGATGAGGCTGACTATTACTGTCAGGCGTGGGACACCAGC
ACTGCTGTCTTCGGAAGTGGGACCAAGCTCACCGTCCTA

Amino acid sequence of a variant of clone 15.186.35 scFv against N-terminus fragment of human CCR5 [SEQ ID NO: 25]:

QVTLKESGPTLVKPTQTLTLTCTLSGFSLSSTSGVSVGWIRQPPGKALEWLASINWNDDKCYSPSLKSRLTITKDTPKNQV
VLAMSNMDPADTATYSCALDMPPHDSGPQSFDASDVWGPMTMTVSSGGGGSGGGGSGGGGSGGGGSSYELMQLPSVSVS
PGQTASITCSGDNLGDKYACWYQQKPGRSPVLVIYGNKRPSGIPERFSGSNSGNTATLTISGTQAMDEADYYCQAWDTS
TAVFGTGTCLTVL

DNA sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 26]:

CAGGTGCAGCTGCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCGGAGACCCTGTCCCTCACTTGCACTGTCTCTGGTGG
CTCCATCGGTCATGACTACTGGAGCTGGATACGGCAGCCCCCAGGGGAGGGACTGGAGTGGATTGGTTTCATCTTCTTCG
ATGGGAGCACCAACTACAACCCCTCCCTCAACGGTCGAGtCACCATCTCACTCGACACGTGGAAGAATCAGCTCTCCCTG
AGGCTGACCTCTGTGACCGCTGCGGACACGGCCGTGTATTTCTGTGCGAGACTAAAGGGGGCGTGGTTATTGTCTGAACC
CCCTTACTTCAGCTCCGACGGCATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAGGCGGTGGTGGATCAG
GCGGCGGAGGATCTGGCGGAGGTGGCAGCGGTGGTGGAGGCAGTAATTTTATGCTGACTCAGCCCCCCTCAGCGTCTGGG
ACCCCCGGGCAGAGGGTCAGCATCTCTTGTCTGGGAGCAGCTCCGACATCGGAAGTAATACTGTAAACTGGTACCAGCA
ACTCCAGGAACGGCCCCCAAACCTCCTCATCTATAGTAATAATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCT
TCAAGTCTGGCACCTCAGCCTCCCTGGTCATCAGTGGCCTCCAGTCTGAGGATGAGGCTGATTATTATTGTGCAGCATGG
GATGAGAGCCTGAATGGTGTGGTGTTCGGCGGAGGAACCAAGGTGACCGTCCTA

Amino acid sequence of a variant of clone 15.150.11 scFv against loop 6 fragment of human CCR5 [SEQ ID NO: 27]:

QVQLQESGPGLVKPSETLSLTCTVSGGSIGHDYWSWIRQPPGEGLEWIGFIFFDGSTNYNPSLNGRVTISLDTSKNQLSL
RLTSVTAADTAVYFCARLKGAWLLSEPPYFSSDGMVDVWGQGTVTTVSSGGGGSGGGGSGGGGSGGGGSGNFMILTQPPSASG
TPGQRVSISSGSSSDIGSNTVNWYQQLPGTAPKLLIYSNNQRPSGVPDRFSGFKSGTSASLVISGLQSEDEADYYCAAW
DESLNGVVFGGGTKVTVL

FIGURE 2A

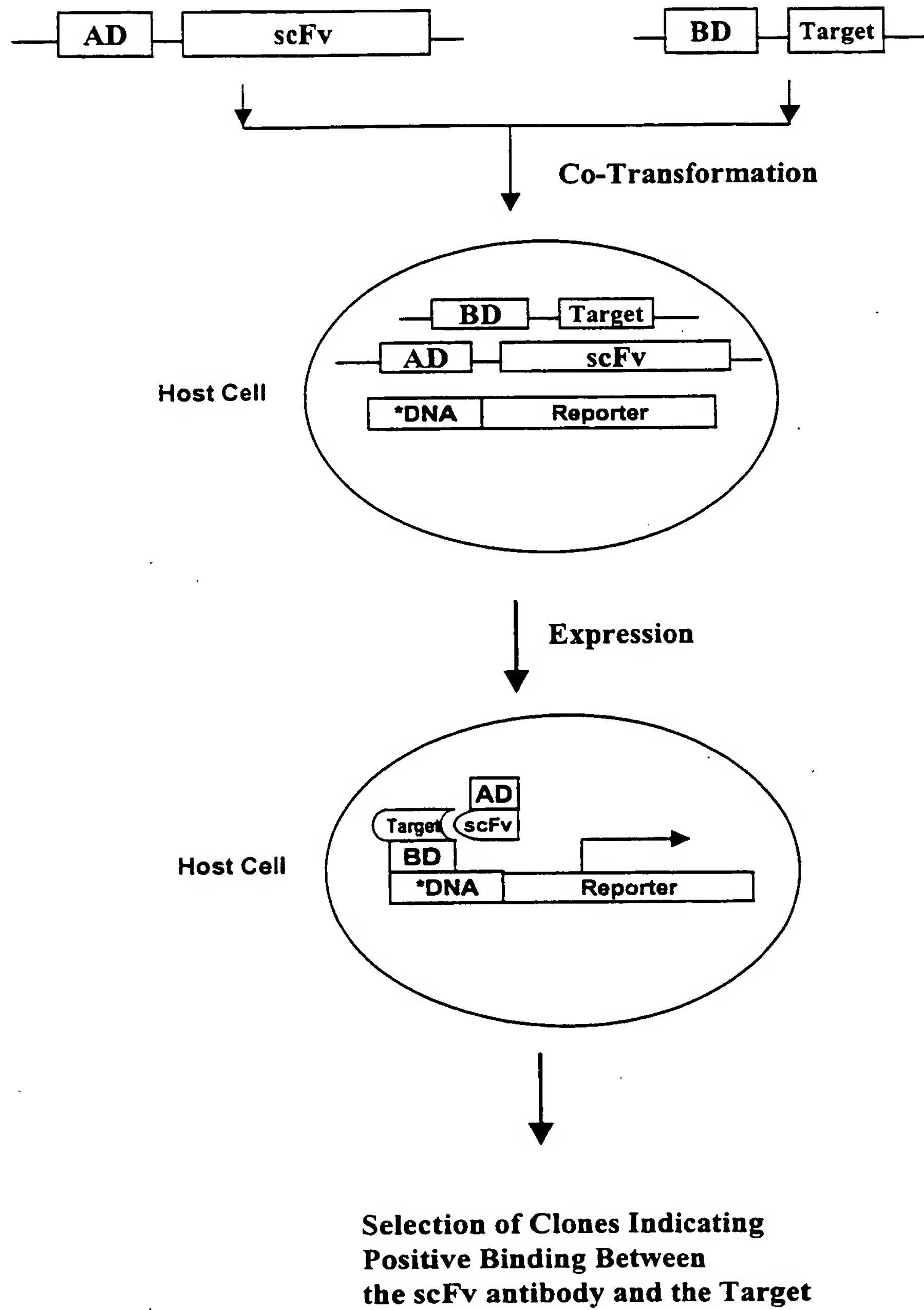


FIGURE 2B

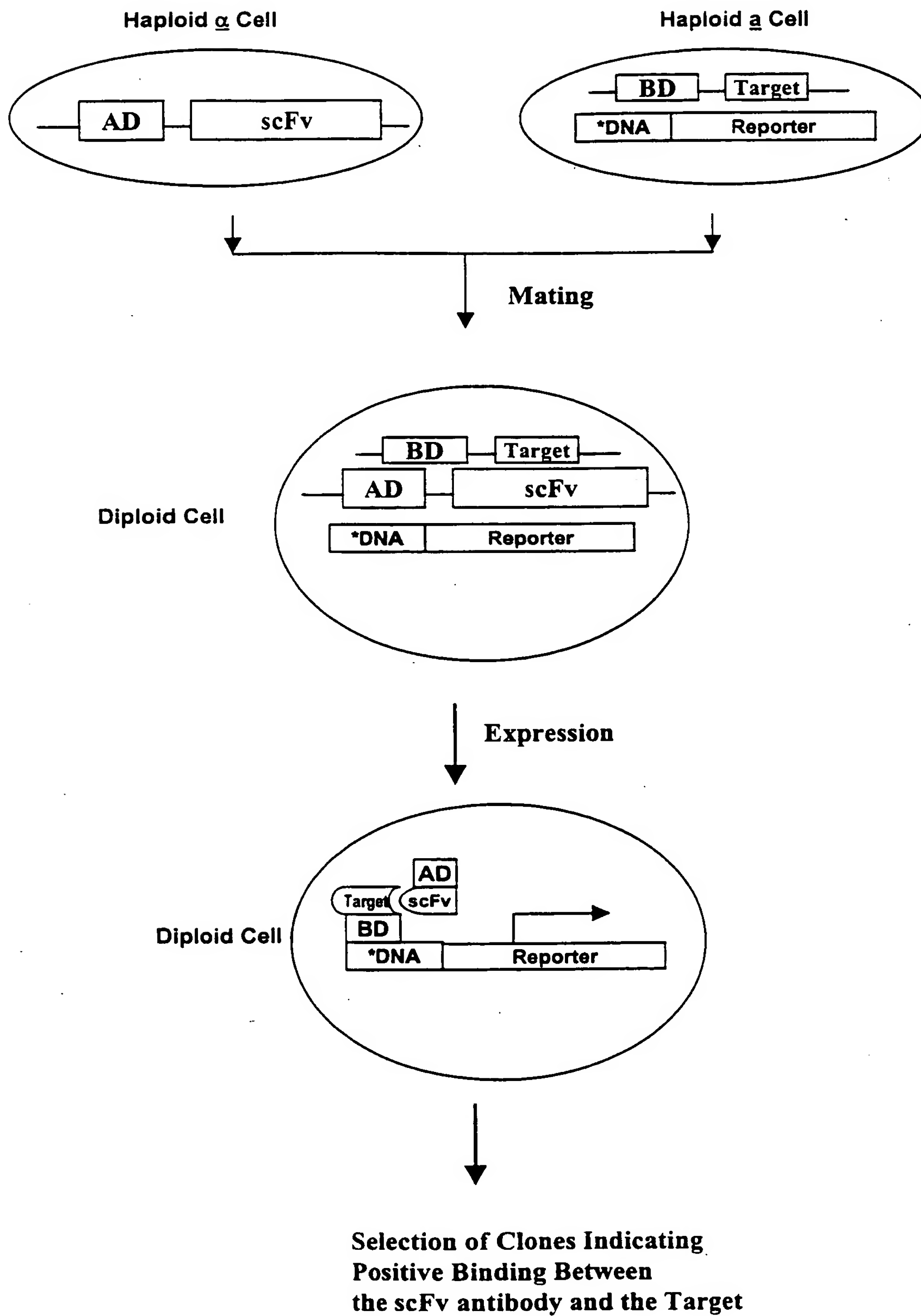


FIGURE 3

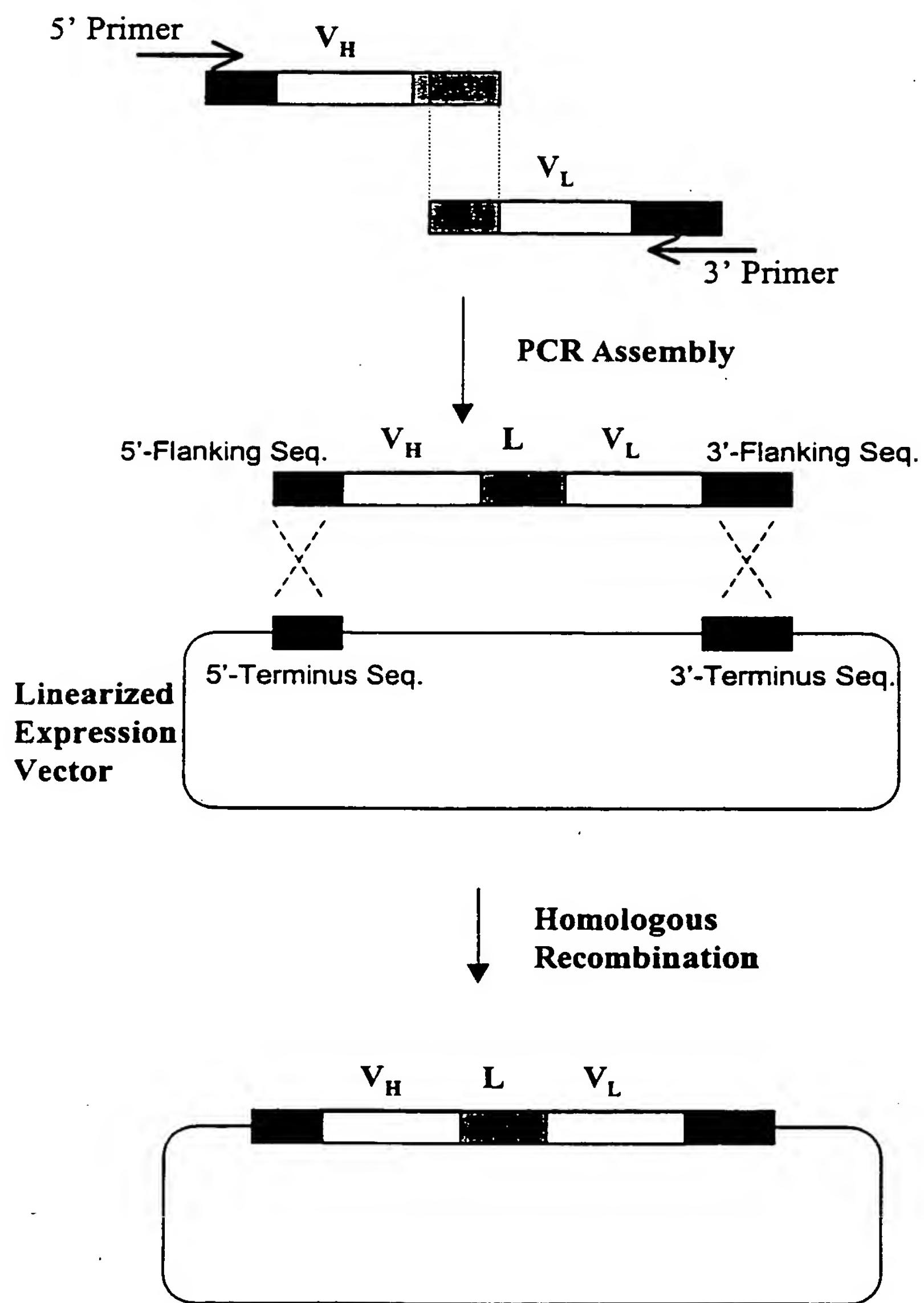


FIGURE 4

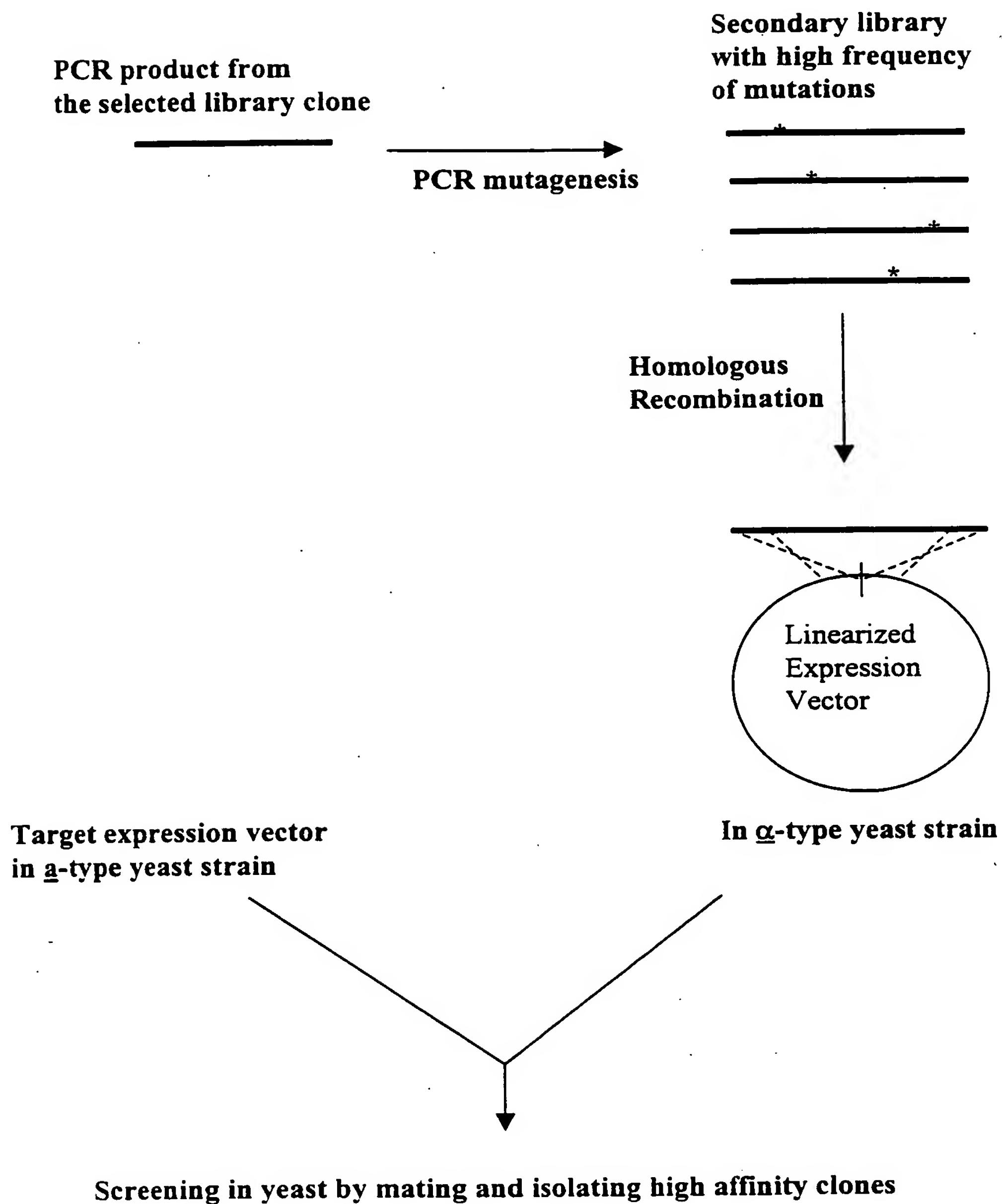


FIGURE 9A

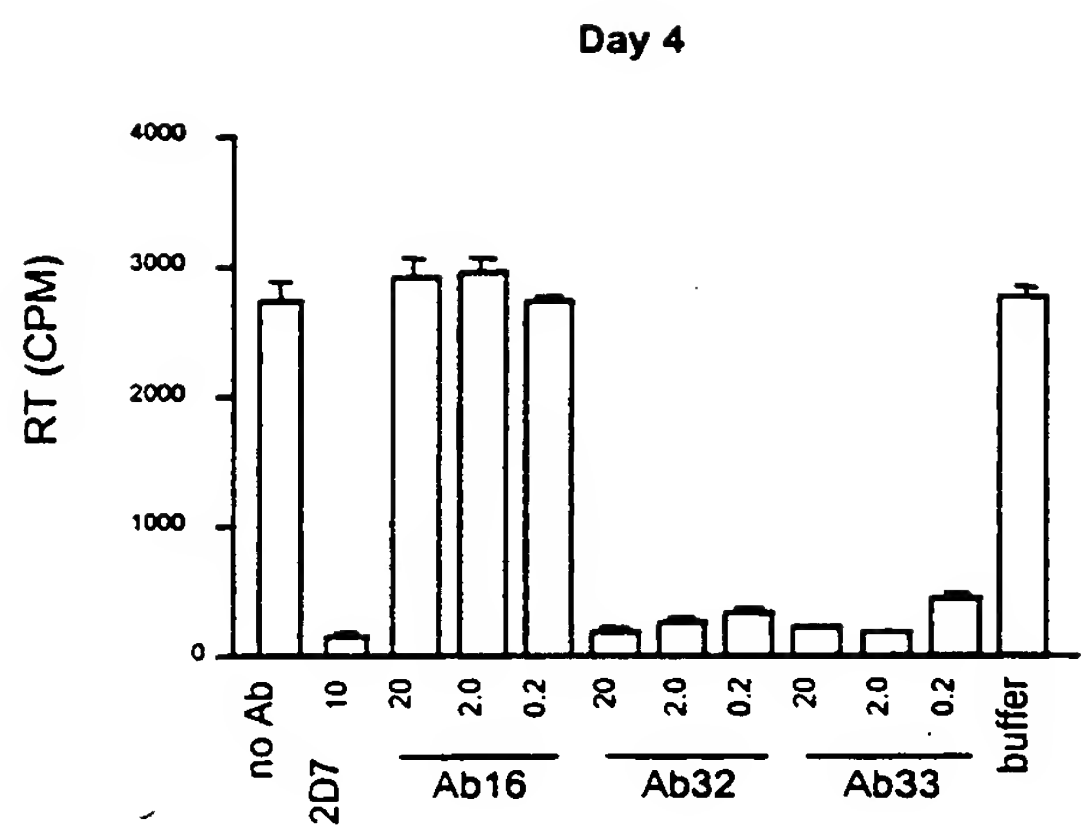


FIGURE 9B

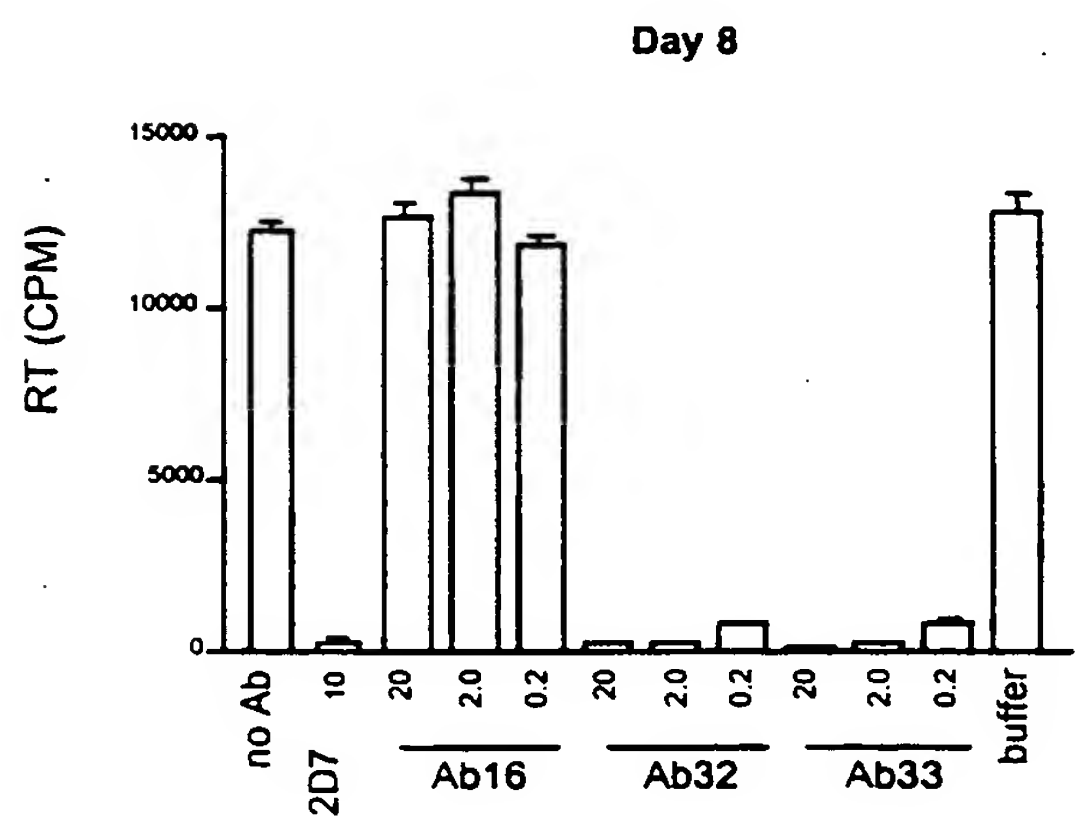
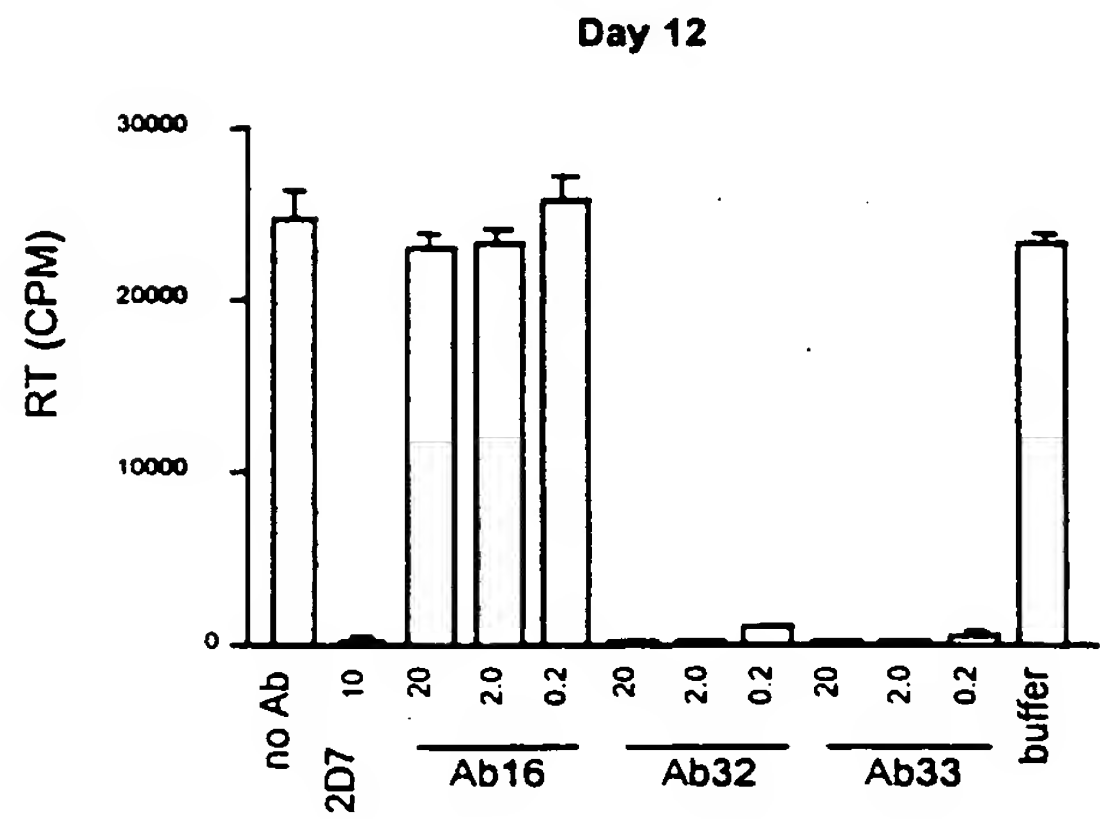


FIGURE 9C



2007-10-20 10:22:00

FIGURE 10A

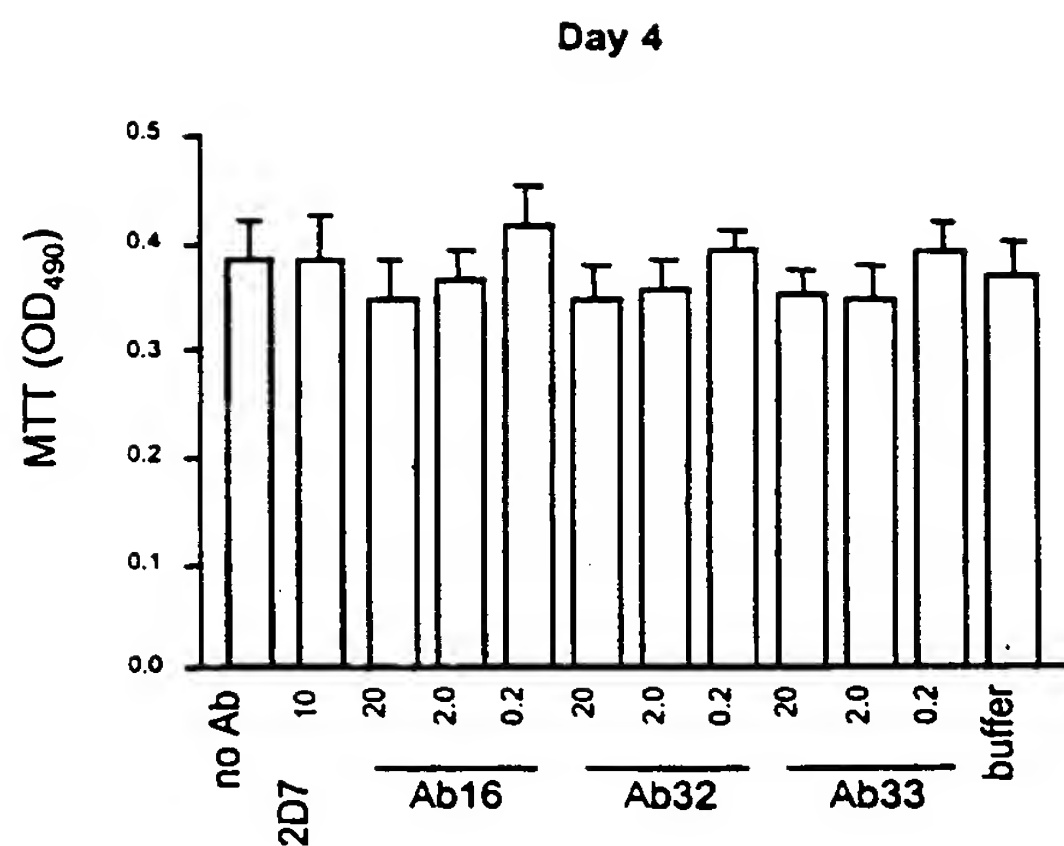


FIGURE 10B

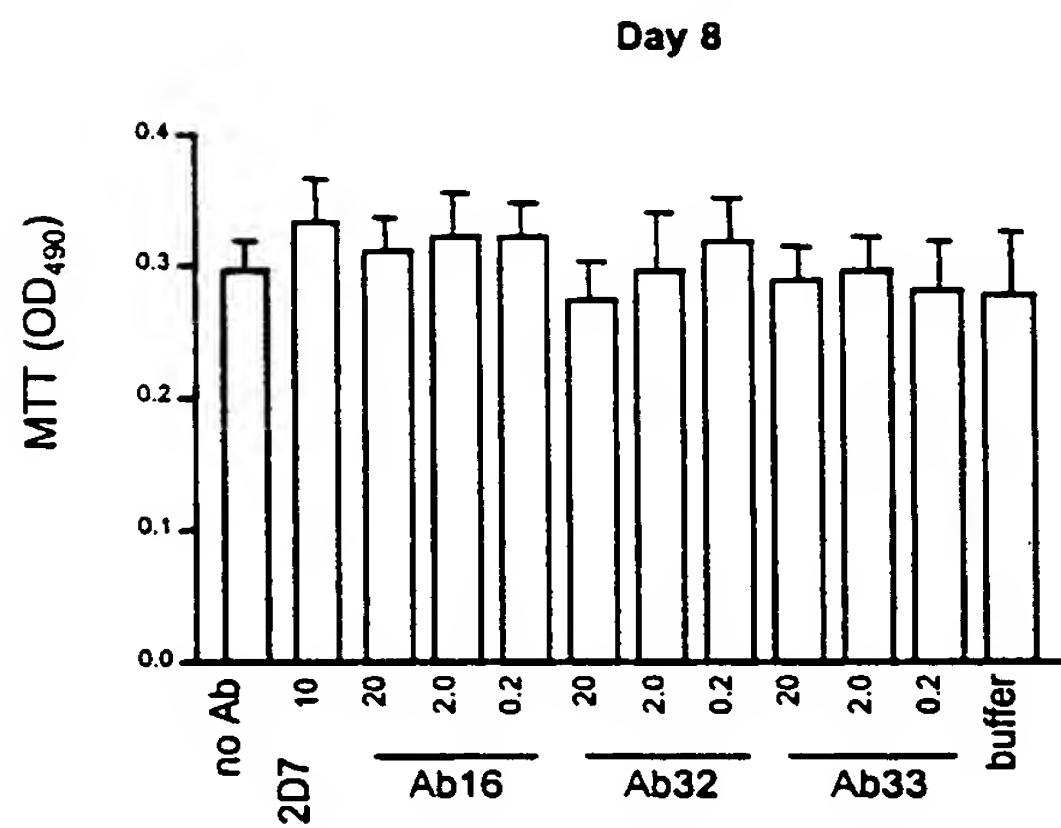


FIGURE 10C

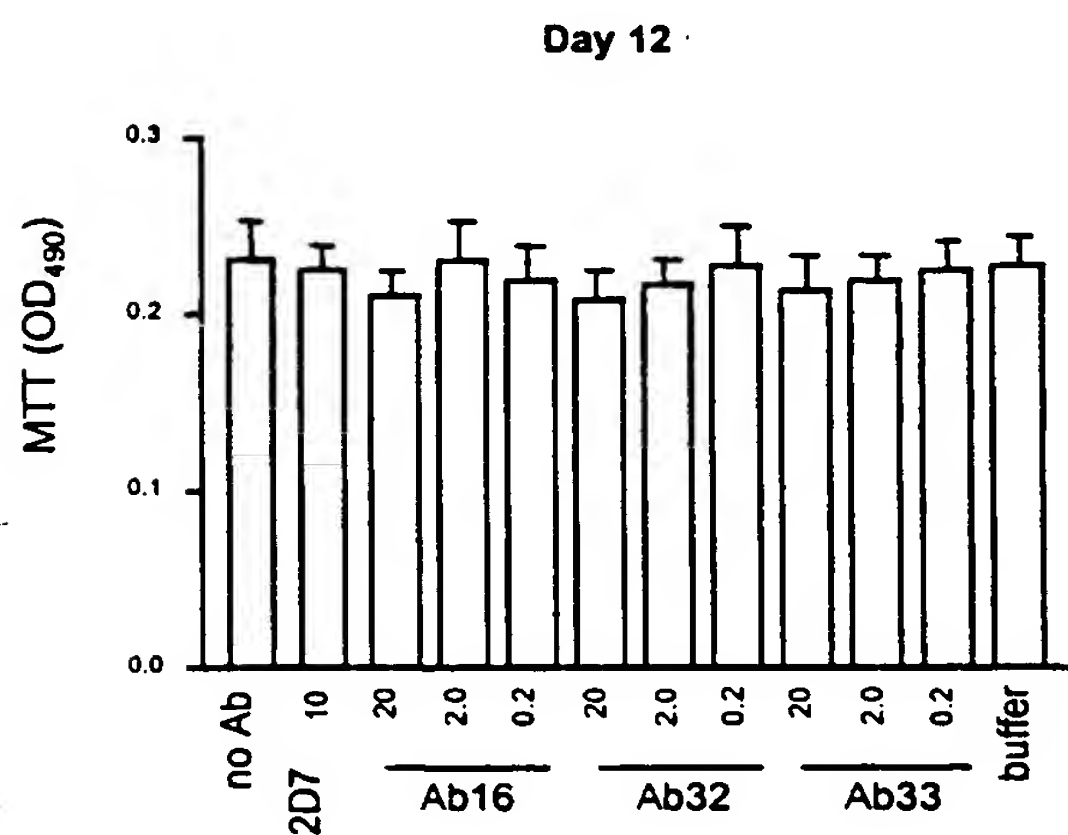


FIGURE 11A

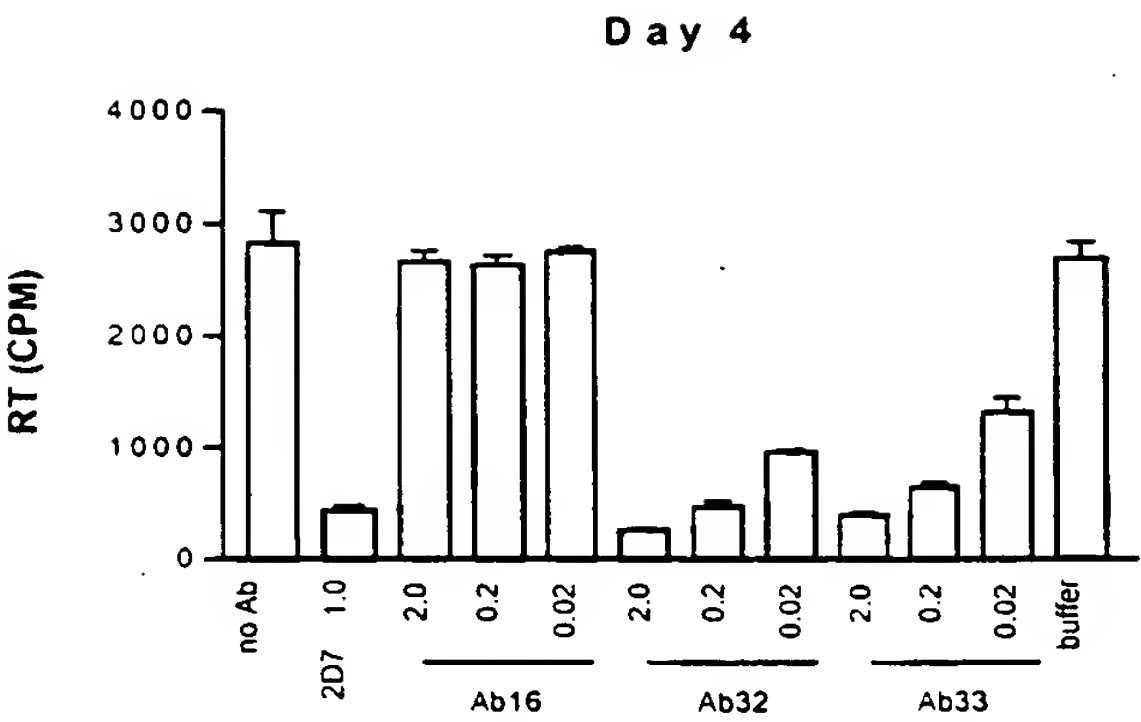


FIGURE 11B

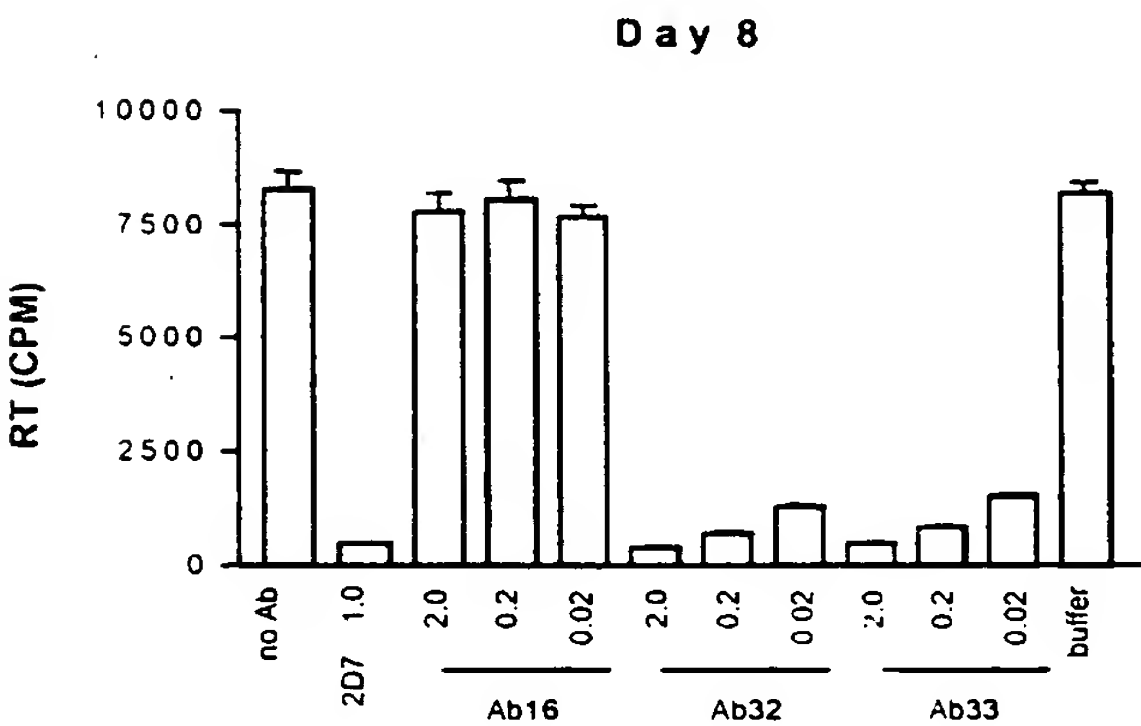


FIGURE 11C

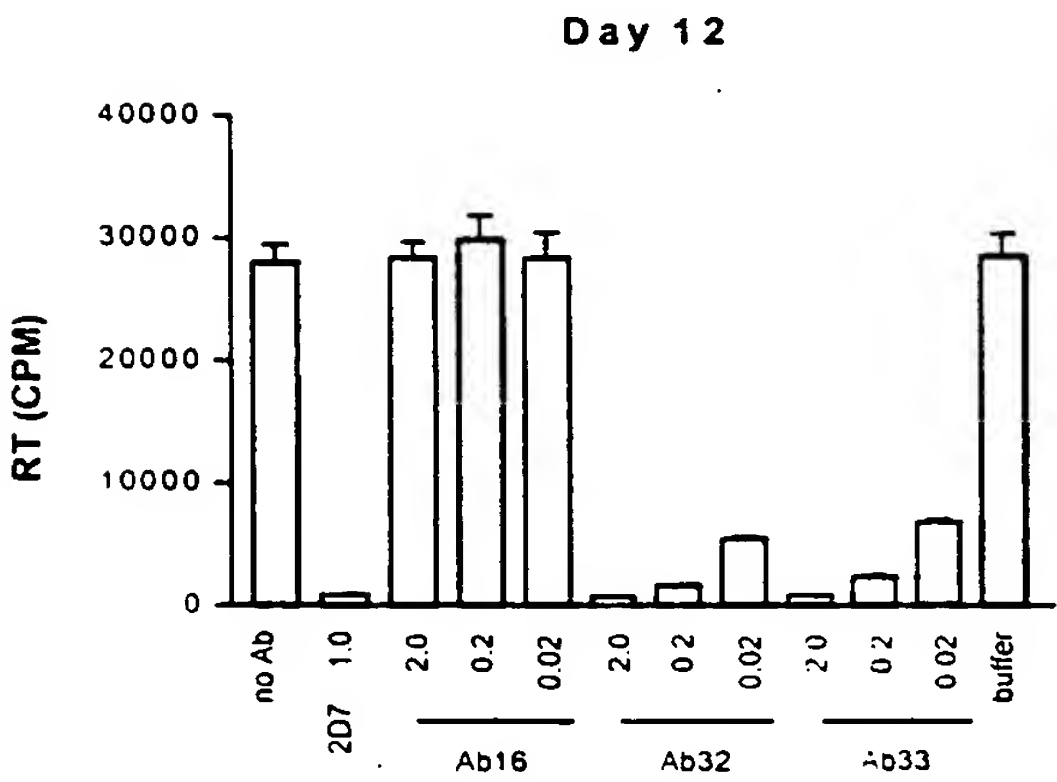




FIGURE 12

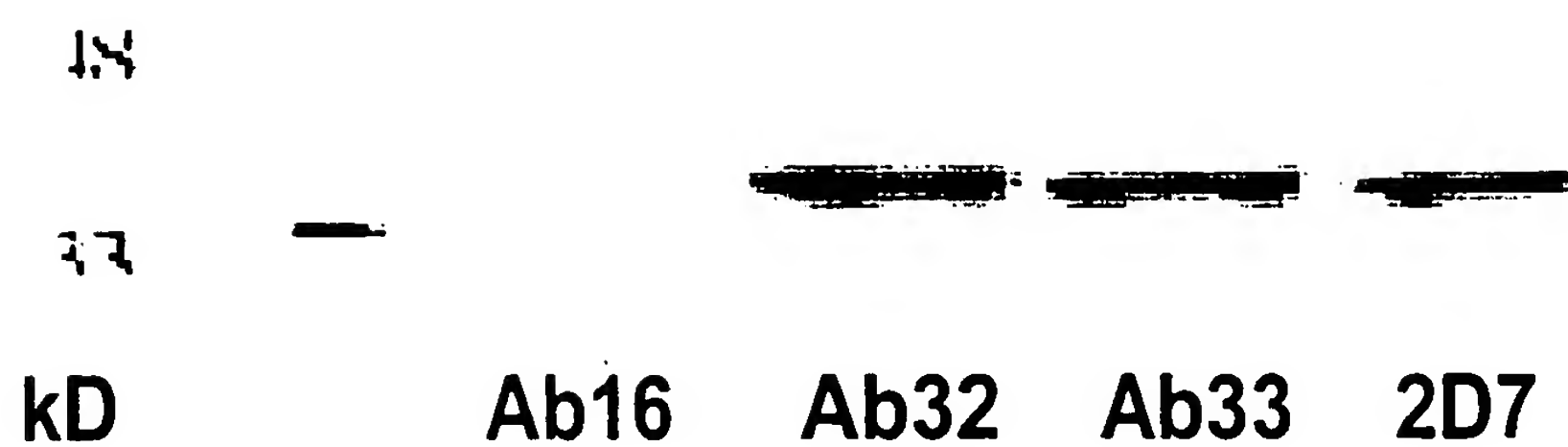


FIGURE 13

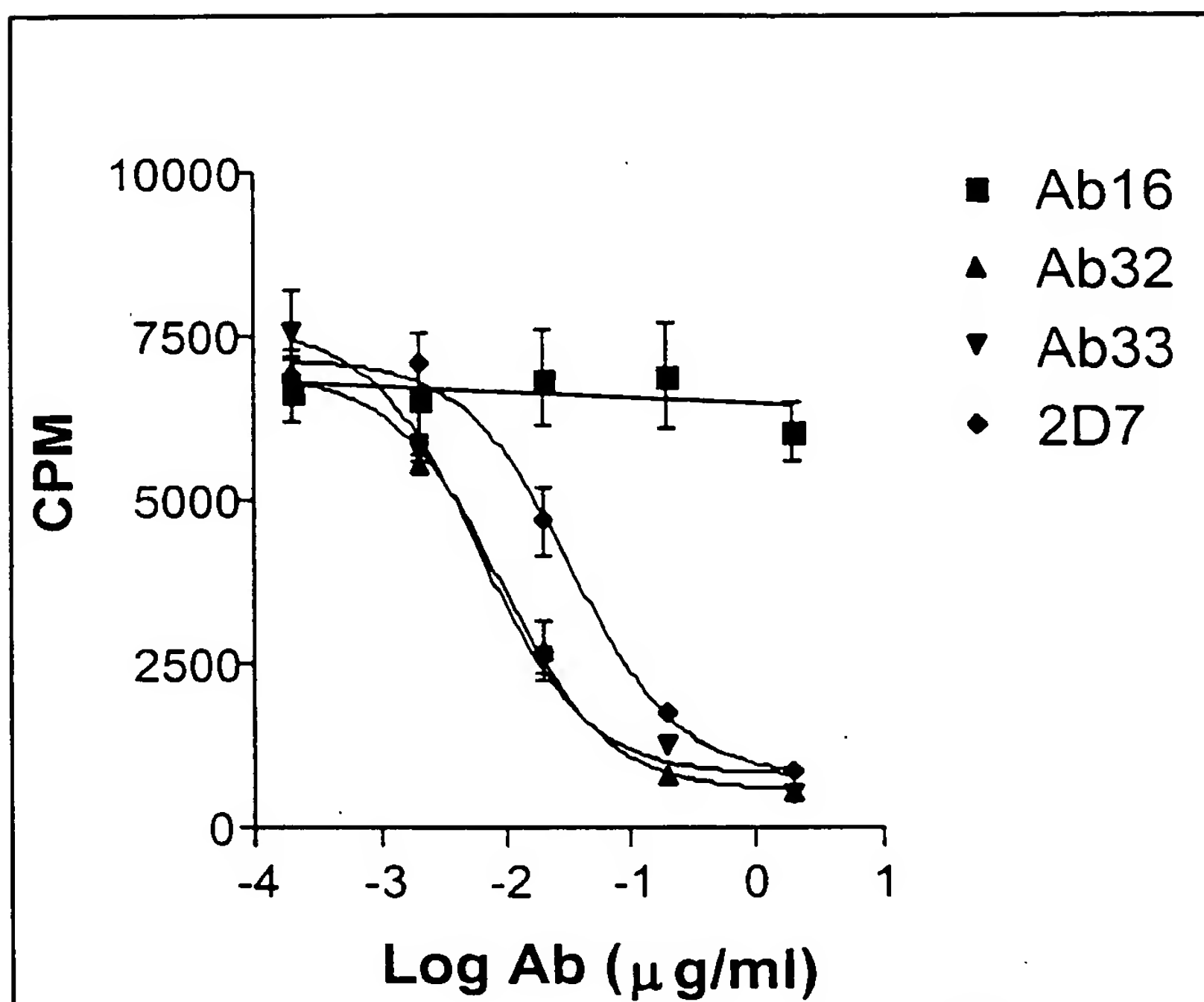


FIGURE 14

